Trends and outcomes of transarterial chemoembolization in hepatocellular carcinoma: a national survey

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BACKGROUND: Transarterial chemoembolization (TACE) is a palliative procedure frequently used in patients with advanced hepatocellular carcinoma (HCC). We examined the national inpatient trends of TACE and related outcomes in the United States over the last decade.

METHODS: We utilized the National Inpatient Sample (2002 to 2012) and performed trend analyses of TACE for HCC in all adult patients (age >18 years). Multivariate analyses for the outcomes of in-hospital "procedure-related complications" (PRCs) and "post-procedure complications" (PPCs) were performed. We also compared early (2002 to 2006) and late (2007 to 2012) eras by multivariate analyses to identify predictors of complications, healthcare resource utilization and mortality.

RESULTS: Overall, 19058 patients underwent TACE for HCC where PRCs and PPCs were seen in 24.2% and 17.6% of patients, respectively. The overall trends in the use of TACE (P<0.001) and associated PRCs (P=0.006) were observed to be increasing. There was less mortality [adjusted Odds ratio (aOR): 0.58; 95% CI: 0.41, 0.82], reduced length of hospital stay (-1.87 days; 95% CI: -2.77, -0.97) and increased hospital charges ($19232; 95% CI: 11013, 27451) in the late era. Additionally, there was increased mortality (aOR: 4.07; 95% CI: 2.96, 5.59), PRCs (aOR: 3.21; 95% CI: 2.56, 4.02), and PPCs (aOR: 2.70; 95% CI: 2.11, 3.46) among patients with coagulopathy.

CONCLUSIONS: There is an increasing trend of TACE utilization in HCC. However, the outcomes are worse in patients with coagulopathy. Although PRCs have increased, mortality has decreased in recent years. These findings should be considered during TACE evaluation in patients with HCC.

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KEY WORDS: transarterial chemoembolization; hepatocellular carcinoma; procedural complications; mortality

Introduction

The incidence of hepatocellular carcinoma (HCC) in the United States has increased within the last two decades for a multitude of reasons. There are an increasing number of patients with longstanding chronic hepatitis C, a large influx of immigrants from East Asia and other endemic geographic areas of hepatitis B and C, and the emergence of nonalcoholic fatty liver disease.[1-4] Additional reasons also include limited availability and poor compliance with HCC screening programs, as well as delay in treatment strategies.[5] In fact, over 60% to 70% of patients with HCC are diagnosed at a late-stage or have other contraindications that preclude curative therapies such as surgical resection, radiofrequency ablation, and liver transplantation.[6] A feasible option for these patients is transarterial chemoembolization (TACE), which should be considered for individuals with both large or multinodular tumors and a good performance status.[7]

Outcomes of TACE have been reported from high-vol-

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ume, single-center studies in selected groups of patients with compensated liver disease and show improved survival compared to supportive care for unresectable HCC.[8, 9] A systematic review of randomized trials in compensated liver disease also demonstrated that patient survival is significantly improved with TACE.[9] Generally, patients with decompensated liver disease in the form of severe coagulopathy, ascites, portal vein thrombosis, or extrahepatic tumor spread are excluded from these trials. While procedure related mortality (0-3%) has decreased,[10-13] some researchers have reported complications of TACE including hepatic injury/failure (7%), gastro-duodenal ulcerations (5%), hepatic abscess (2%), intraoperative hemorrhage or injury to surrounding structures (<2%), iatrogenic pneumothorax (2%), and biliary tract injuries (0.5%-2%).[14]

Over the last decade, there is an increasing incidence of patients with incurable HCC in the United States.[15, 16] This may imply an increasing need for TACE, which has not been analyzed from population databases. Thus, we utilized the National Inpatient Sample (NIS) database to study the trends of TACE and related outcomes in patients with HCC. Additionally, we sought to evaluate key determinants that impact TACE-related outcomes.

Methods

Database information

The NIS database is the largest, multi-institutional, publicly available database in the United States, representing an approximate 20% stratified sample of non-federal hospitals in 47 states. It contains data from over 8 million hospital stays each year and allows users to track and analyze trends and outcomes of health care. We analyzed the NIS database from years 2002 to 2012 among all inpatient adults (age >18 years) with a principal diagnosis of HCC (ICD-9 code: 155.0--A diagnosis code determined by International Classification of Disease-Clinical Modification, Ninth Revision, [ICD-CM] codes). According to weighted estimate, 19058 adult patients were identified who underwent TACE for HCC with ICD-CM procedure code (38.80, 38.86, 99.25, 38.91, 88.47).

The NIS database has limited clinical variables, but it provides a large sample size representative of the United States. Moreover, it is reliable in terms of hard end-points such as inpatient mortality and length of hospital stay. Another unique feature of this database is information on the direct charges for hospital stay, which have not been studied in the past among patients with TACE for HCC. Additional data collected including healthcare utilization were, age, gender, race, income (National Quartile), type of insurance, type of hospital (rural/urban non-teaching vs urban teaching), hospital size, hospital region, and Elixhauser index.[17]

Outcome variables

We studied TACE-associated procedure-related complications (PRCs) and post-procedure complications (PPCs) in patients who underwent TACE for HCC. PRCs included hepatic failure, intraoperative hemorrhage or injury to surrounding structures, iatrogenic pneumothorax, intraabdominal or hepatic abscess, need for endoscopic biliary intervention, and transfusion. These above PRCs were defined based on previous literature and identified by the presence of secondary ICD-9-CM diagnostic and procedure codes.[14, 18] TACE-associated PPCs were identified based on previously reported ICD-9-CM coding algorithm and by use of claims data, which has a high positive predictive value.[19-21] These data included cardiac complications, deep vein thrombosis, mechanical wound complications, pneumonia, pulmonary failure, paralytic ileus, pulmonary emboli, renal failure, sepsis, urinary infections, and in-hospital mortality. We divided the HCC patients who underwent TACE into two time intervals--2002 to 2006 (early) and 2007 to 2012 (late) and studied the mortality, length of hospital stay, and total charges amongst the two periods. Severity of liver disease is assessed with the help of various parameters and scoring systems. Two of the most commonly used scoring systems are Child-Turcotte-Pugh and model for end-stage liver disease (MELD) scores. The majority of variables involved in calculating these scores are not part of the NIS database. However, an indirect measure of international normalized ratio (INR), which is part of both scoring system, was represented in NIS database as presence or absence of coagulopathy. Coagulopathy and other comorbidities were defined based on NIS comorbidity measures assigned using the Agency for Healthcare Research and Quality (AHRQ) comorbidity software, developed by Elixhauser et al, using ICD-9-CM diagnoses and Diagnosis Related Group (DRG) in effect on the discharge date.[22] The definition of coagulopathy included the following discharge ICD-9-CM diagnosis codes: 286.0-286.9, 287.1, 287.3-287.5 and 289.81-289.82, and excluded the following discharge DRGs: pre-V25 DRG (397) and V25-V29 DRGs (813).[22] Therefore, we analyzed the outcomes of TACE in patients with and without coagulopathy.

Statistical analysis

SAS 9.4 (SAS Institute, Cary, NC) was used to perform all analyses, employing appropriate survey estimation commands and strata weights. Weighted frequencies and percentages were calculated for all categorical vari-